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**Amendment and Response**

Serial No.: 10/008,355

Confirmation No.: 4382

Filed: November 8, 2001

For: DIPEPTIDYLPEPTIDASES AND METHODS OF USE**OFFICIAL****Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-53. (Canceled)

54. (New) An isolated nucleic acid, the complement of which hybridizes to SEQ ID NO:1 under hybridization conditions of 0.5 M phosphate buffer, pH 7.2, 7% SDS, 10 mM EDTA, at 68°C, followed by three washes for 20 minutes each in 2x SSC, and 0.1% SDS, at 65°C;

wherein the isolated nucleic acid encodes a protein having dipeptidylpeptidase amidolytic activity; and

wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the unblocked amino-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the  $\alpha$ -carbon atom of the second amino acid from the unblocked amino-terminal end of the polypeptide, with the proviso that the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged.

55. (New) The isolated nucleic acid of claim 54 wherein the protein is a protease from a gram-negative bacterium.

56. (New) The isolated nucleic acid of claim 55 wherein the protein is a protease from *Porphyromonas gingivalis*.

57. (New) The isolated nucleic acid of claim 54 having a nucleotide sequence comprising SEQ ID NO:1.

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58. (New) The isolated nucleic acid of claim 54 wherein the protein encoded by the nucleic acid has a percentage amino acid identity of greater than 40% with SEQ ID NO:2;  
wherein the protein comprises the sequence TGGNSGSPVF (SEQ ID NO:25); and  
wherein the percentage amino acid identity is determined by placing the TGGNSGSPVF residues of the protein in register with residues 644-653 of SEQ ID NO:2.
59. (New) The isolated nucleic acid of claim 54 wherein the nucleic acid encodes a protein comprising SEQ ID NO:2.
60. (New) An isolated nucleic acid encoding a protein having dipeptidylpeptidase amidolytic activity;  
wherein the protein has a sequence comprising the residues 543 to 712 of SEQ ID NO:2;  
and  
wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the unblocked amino-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the  $\alpha$ -carbon atom of the second amino acid from the unblocked amino-terminal end of the polypeptide, with the proviso that the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged.
61. (New) The isolated nucleic acid of claim 60, wherein the protein has a sequence comprising residues 540 to 712 of SEQ ID NO:2.
62. (New) The isolated nucleic acid of claim 61, wherein the protein has a sequence comprising residues 522 to 712 of SEQ ID NO:2.

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63. (New) An isolated nucleic acid encoding a protein having SEQ ID NO:2 or variants thereof;

wherein the protein and variants thereof have a percentage amino acid identity of greater than 40% with SEQ ID NO:2;

wherein the protein and variants thereof have dipeptidylpeptidase amidolytic activity;

wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the unblocked amino-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the  $\alpha$ -carbon atom of the second amino acid from the unblocked amino-terminal end of the polypeptide, with the proviso that the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged;

wherein the protein and variants thereof comprise the sequence TGGNSGSPVF (SEQ ID NO:25); and

wherein the percentage amino acid identity is determined by placing the TGGNSGSPVF residues of the protein in register with residues 644-653 of SEQ ID NO:2.

64. (New) The isolated nucleic acid of claim 63 wherein the protein is a protease from a gram-negative bacterium.

65. (New) The isolated nucleic acid of claim 64 wherein the protein is a protease from *Porphyromonas gingivalis*.

66. (New) The isolated nucleic acid of claim 63 wherein the protein and variants thereof have a percentage amino acid identity of greater than 50% with SEQ ID NO:2.

67. (New) The isolated nucleic acid of claim 66 wherein the protein and variants thereof have a percentage amino acid identity of greater than 60% with SEQ ID NO:2.

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68. (New) The isolated nucleic acid of claim 67 wherein the protein and variants thereof have a percentage amino acid identity of greater than 70% with SEQ ID NO:2.

69. (New) The isolated nucleic acid of claim 68 wherein the protein and variants thereof have a percentage amino acid identity of greater than 80% with SEQ ID NO:2.

70. (New) The isolated nucleic acid of claim 69 wherein the protein and variants thereof have a percentage amino acid identity of greater than 90% with SEQ ID NO:2.

71. (New) An isolated nucleic acid comprising a nucleotide sequence having at least about 70% identity with SEQ ID NO:1;

wherein the nucleotide sequence encodes a protein having dipeptidylpeptidase amidolytic activity; and

wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the unblocked amino-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the  $\alpha$ -carbon atom of the second amino acid from the unblocked amino-terminal end of the polypeptide, with the proviso that the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged.

72. (New) The isolated nucleic acid of claim 71 wherein the nucleotide sequence has at least about 80% identity with SEQ ID NO:1.

73. (New) The isolated nucleic acid of claim 72 wherein the nucleotide sequence has at least about 90% identity with SEQ ID NO:1.

74. (New) The isolated nucleic acid of claim 73 wherein the nucleotide sequence has at least about 95% identity with SEQ ID NO:1.

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75. (New) An isolated nucleic acid comprising a nucleotide sequence having at least about 70% identity with SEQ ID NO:1;

wherein the nucleotide sequence encodes a protein having SEQ ID NO:2 or variants thereof;

wherein the protein and variants thereof have a percentage amino acid identity of greater than 40% with SEQ ID NO:2;

wherein the protein and variants thereof have dipeptidylpeptidase amidolytic activity;

wherein the dipeptidylpeptidase amidolytic activity is defined as activity for cleaving the peptide bond between the second and the third amino acids from the unblocked amino-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the  $\alpha$ -carbon atom of the second amino acid from the unblocked amino-terminal end of the polypeptide, with the proviso that the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged;

wherein the protein and variants thereof comprise the sequence TGGNSGSPVF (SEQ ID NO:25); and

wherein the percentage amino acid identity is determined by placing the TGGNSGSPVF residues of the protein in register with residues 644-653 of SEQ ID NO:2.

76. (New) An isolated nucleic acid consisting of nucleotide sequence SEQ ID NO:1.

77. (New) An isolated nucleic acid encoding a protein consisting of SEQ ID NO:2